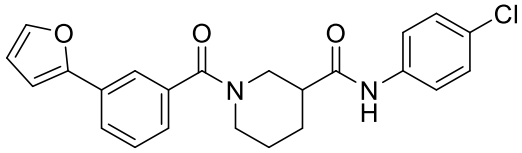
Product data sheet

MedKoo Cat#: 531658 Name: CCG-203971 CAS#: 1443437-74-8 Chemical Formula: $C_{23}H_{21}ClN_2O_3$ Exact Mass: 408.1241 Molecular Weight: 408.88	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
CCG-203971 is an inhibitor of SRE activation in the prostate cancer cell line PC-3 (IC50 = 6.4 μM), with 87% inhibition of SRE activation achieved at 100 μM. This compound also inhibits PC-3 cell migration (IC50 = 4.2 μM), as determined by a scratch wound assay

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	81	198.10

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.45 mL	12.23 mL	24.46 mL
5 mM	0.49 mL	2.45 mL	4.89 mL
10 mM	0.24 mL	1.22 mL	2.45 mL
50 mM	0.05 mL	0.24 mL	0.49 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Yu-Wai-Man C, Spencer-Dene B, Lee RMH, Hutchings K, Lisabeth EM, Treisman R, Bailly M, Larsen SD, Neubig RR, Khaw PT. Local delivery of novel MRTF/SRF inhibitors prevents scar tissue formation in a preclinical model of fibrosis. Sci Rep. 2017 Mar 31;7(1):518. doi: 10.1038/s41598-017-00212-w. PMID: 28364121; PMCID: PMC5428058.

2. Haak AJ, Tsou PS, Amin MA, Ruth JH, Campbell P, Fox DA, Khanna D, Larsen SD, Neubig RR. Targeting the myofibroblast genetic switch: inhibitors of myocardin-related transcription factor/serum response factor-regulated gene transcription prevent fibrosis in a murine model of skin injury. J Pharmacol Exp Ther. 2014 Jun;349(3):480-6. doi: 10.1124/jpet.114.213520. Epub 2014 Apr 4. PMID: 24706986; PMCID: PMC4019321.

In vivo study

1. Haak AJ, Tsou PS, Amin MA, Ruth JH, Campbell P, Fox DA, Khanna D, Larsen SD, Neubig RR. Targeting the myofibroblast genetic switch: inhibitors of myocardin-related transcription factor/serum response factor-regulated gene transcription prevent fibrosis in a murine model of skin injury. J Pharmacol Exp Ther. 2014 Jun;349(3):480-6. doi: 10.1124/jpet.114.213520. Epub 2014 Apr 4. PMID: 24706986; PMCID: PMC4019321.

2. Hutchings KM, Lisabeth EM, Rajeswaran W, Wilson MW, Sorenson RJ, Campbell PL, Ruth JH, Amin A, Tsou PS, Leipprandt JR, Olson SR, Wen B, Zhao T, Sun D, Khanna D, Fox DA, Neubig RR, Larsen SD. Pharmacokinetic optimitzation of CCG-203971: Novel inhibitors of the Rho/MRTF/SRF transcriptional pathway as potential antifibrotic therapeutics for systemic scleroderma. Bioorg Med Chem Lett. 2017 Apr 15;27(8):1744-1749. doi: 10.1016/j.bmcl.2017.02.070. Epub 2017 Mar 10. PMID: 28285914; PMCID: PMC5395305.

7. Bioactivity

Biological target:

CCG-203971 is a second-generation Rho/MRTF/SRF pathway inhibitor. CCG-203971 potently targets RhoA/C-activated SRE-luciferase (IC50 =6.4 μM). CCG-203971 inhibits PC-3 cell migration with an IC50 of 4.2 μM.

In vitro activity

Candidate MRTF/SRF pathway inhibitor, CCG-203971, was tested using a functional three-dimensional fibroblast-populated collagen contraction assay. This assay was chosen as it has been shown to be a good in vitro model to study tissue contraction. CCG-203971 decreased collagen matrix contraction in a concentration-dependent manner but CCG-222740 was five times more potent than CCG-203971 in human conjunctival fibroblasts [IC50 = 5 μM compared to 25 μM] (Fig. 1A and B). These results were confirmed in rabbit conjunctival fibroblasts, where CCG-222740 was similarly more effective at decreasing collagen matrix contraction than CCG-203971 (Fig. 2A and B). In addition, CCG-222740 was less cytotoxic than CCG-203971 with a cell viability of 100% at 10 μM, 88% at 30 μM, and 85% at 100 μM (Fig. 1C). How CCG-222740 and CCG-203971 affect the activity of an SRF reporter gene was also compared in transfected cells. Both compounds showed similar activity, with almost 100% inhibition of baseline reporter activity (Figs 1D and 2E,F). However, examination of endogenous gene expression revealed that CCG-222740 was a more potent inhibitor of expression for two MRTF/SRF target genes classically linked to fibrosis (ACTA2, coding for alpha-smooth muscle actin – αSMA; and CTGF, coding for Connective Tissue Growth Factor) (Fig. 1E–H). CCG-222740 also decreased ACTA2 gene expression to a greater extent than CCG-203971 in rabbit conjunctival fibroblasts (Fig. 2C and D).

Reference: Sci Rep. 2017 Mar 31;7(1):518. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28364121/

In vivo activity

To determine whether these effects would translate in vivo, CCG-203971 was tested in a bleomycin skin injury model. Because of its modest solubility, bleomycin was administered in 50 μl of DMSO intraperitoneally. Preliminary studies showed that the compound administered in this manner was well tolerated at 100 mg/kg twice a day. Intradermal bleomycin for 2 weeks along with the DMSO control (50 μl i.p.) resulted in marked dermal thickening ($P < 0.0001$) compared with the PBS+DMSO group, which did not receive bleomycin (Fig. 5, A–B). CCG-203971 treatment strongly and significantly ($P < 0.001$) suppressed the bleomycin-induced skin thickening in this model (Fig. 5, A–B). Skin collagen amounts, assessed by measurement of hydroxyproline content, showed similar results. Bleomycin injections promoted collagen deposition ($P < 0.01$) and CCG-203971 was able to block this effect ($P < 0.05$, Fig. 5C).

Reference: J Pharmacol Exp Ther. 2014 Jun;349(3):480-6. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24706986/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.